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APPLICATION NUMBER: ***60/075,698***
FILING DATE: ***January 21, 1998***
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PRIORITY DOCUMENT

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01/21/98 09:49 U.S. PTO

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. PKP-005-1

In re the application of Kevin Croker, Shane Weber and Seth Taylor

For: GEL PAD ARRAYS ON FLEXIBLE TAPES

Assistant Commissioner For Patents
Box Provisional Patent Application
Washington, DC 20231

CERTIFICATION UNDER 37 CFR 1.10

Date of Deposit: January 21, 1998 Mailing Label Number: EM284 255 250US

I hereby certify that this Cover Sheet for Filing Provisional Application (37 C.F.R. §1.51(2)(i)) and the documents referred to as attached therein are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to the Assistant Commissioner for Patents, Box Provisional Patent Application, Washington, D.C. 20231.

Mark D. Russett
Name of Person Mailing Paper

Signature of Person Mailing Paper

COVER SHEET FOR FILING PROVISIONAL PATENT APPLICATION

Dear Sir:

The accompanying application, entitled GEL PAD ARRAYS ON FLEXIBLE TAPES, is a provisional patent application under 37 C.F.R. §1.51(a)(2) and §1.53(b)(2).

1. ☒ The name(s) and address(es) of the inventor(s) of this application is/are as follows:

	Last Name	First Name	Middle Initial	Residence
1	Croker	Kevin		
2	Weber	Shane		
3	Taylor	Seth		Cambridge, MA
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2. ☐ This invention was made by an agency of the United States Government or under contract with an agency of the United States Government. The name of the U.S. Government agency and the Government contract number are:

Agency:_____

Contract No.:_____

3. ☒ The following documents are enclosed:

- ☒ 4 page(s) of specification
- ☒ 1 sheet(s) of drawings (Fig. 1)
- ☒ 1 page(s) of claims
- ☒ 1 page(s) of abstract

4. ☐ A verified statement to establish small entity status under 37 CFR 1.9 and 1.27 is enclosed.

5. ☐ An Assignment of the invention to _____ is enclosed. A check in the amount of $40.00 for recording this assignment and a recordation form cover sheet (Form PTO 1595) are also enclosed.

6. ☒ The fee for filing this provisional application, as set forth in 37 CFR 1.16(k), is $150.00 .

   a. ☒ A check for this filing fee is enclosed.
   b. ☐ Charge the filing fee to Deposit Account No. 12-0080. (A duplicate copy of this sheet is enclosed.)
   c. ☐ The filing fee is not being paid at this time.

7. ☒ Please charge any fee deficiencies associated with this filing to Deposit Account No. 12-0080. A duplicate copy of this sheet is enclosed.

8. ☒ Please address all future communications to: **Customer Number: 000959** whose address is:

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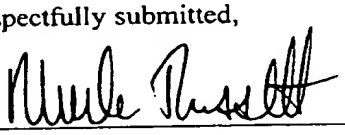
Respectfully submitted,



January 21, 1998
Date

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GEL PAD ARRAYS ON FLEXIBLE TAPES

Related Applications

This application is related to commonly-owned U.S. Provisional Patent Application entitled "Gel Pad Arrays and Methods of Making and Using Them", filed on January 20, 1998. This application is also related to commonly-owned U.S. Provisional Patent Application entitled "Gel Pad Arrays and Methods and Systems For Making Them", filed on even date herewith. The contents of each of these provisional patent applications is hereby incorporated by reference.

Background of the Invention

Microarrays useful for biological analysis have been prepared by immobilizing molecules of biological interest on solid surfaces. However, conventional micro-arrays have certain disadvantages. For example, rigid substrates can be difficult to handle and store.

Summary of the Invention

This invention provides gel pad arrays on a flexible support, such as a flexible tape, and methods for making and using them, and carriers for storing gel pad arrays on tapes. The arrays can be used for sequencing by hybridization (e.g., where the pads include nucleic acid strands immobilized within the gel matrix), for cell based assays (e.g., where the pads include, or are adjacent to and contacting, living cells), and for other uses which will be apparent to one of ordinary skill in the art.

In one aspect, the invention provides flexible tape having a gel pad array disposed on a surface of the tape. In preferred embodiments: the tape comprises means for preventing compression of gel pads when the tape is wound on a reelmore preferably, the means includes at least one ridge which extends along a length of the tape.

In another aspect, the invention provides a carrier for a tape having gel pad arrays thereon. The carrier includes a housing, at least one tape reel for winding the tape, and visible or machine-readable indicia for storing information about the tape stored in the carrier.

Brief Description of the Drawings

Figure 1 depicts a tape according to the invention having a gel pad array thereon.

Detailed Description of the Invention

This invention provides gel pads on flexible tapes, and carriers for such tapes.

The term "gel pad" is known in the art and as used herein refers to a discrete portion of a gel disposed on a substrate such as a solid support, e.g., a plastic, glass, or metal substrate. The substrate can be any support suitable for supporting a gel pad, and can be rigid

(e.g., a glass or plastic plate or sheet) or flexible (e.g., a tape), transparent (e.g., for performing optical measurements through the pad and substrate) or opaque. The properties of the support can be readily selected for use in any particular application. In preferred embodiments, the solid support is substantially non-reactive under conditions used to perform an assay or test procedure with the gel pad or gel pad array. An "array" can be any pattern of spaced-apart gel pads disposed on a substrate; arrays can be conveniently provided in a grid pattern, but other patterns can also be used. In preferred embodiments, a gel pad array according to the invention includes at least about 10 gel pads, more preferably at least about 50, 100, 500, 1000, 5000, or 10000 gel pads. In certain embodiments, the array is an array of gel pads of substantially equal size, thickness, density, and the like, e.g., to ensure that each gel pad behaves consistently when contacted with a test mixture. In certain embodiments, however, the pads of a gel pad array can differ from one another; e.g., a mixed gel pad array can be constructed which includes more than one size or type of gel pad, e.g., gel pads made of different gel materials, or which entrap different species such as reagents or polynucleotide probes. In certain preferred embodiments, gel pads in an array are less than about 1 mm in diameter (or along a side, e.g., in the case of square gel pads), more preferably less than about 500 microns, still more preferably less than about 100, 75, 50, 25, 10, 5, or 1 micron in diameter. Each gel pad can be separated from each neighboring gel pad in the array by at least about 5, 10, 20, 50, 100, or 500 microns.

A gel pad can have any convenient dimension for use in a particular assay. In preferred embodiments, a gel pad is thin enough, and porous enough, to permit rapid diffusion of at least certain reaction components into the gel pad when a solution or suspension is place din contact with the gel pad. For example, in one embodiment, a gel pad array for use in sequencing by hybridization permits polynucleotide fragments from a sample mixture to diffuse (within a conveniently short time period) into the gel pads and hybridize to oligonucleotide capture sequences disposed within the gel pads. In certain preferred embodiments, a gel pad (e.g., in an array of gel pads) has a thickness of at least about 1, 5, 10, 20, 30, 40, 50 or 100 microns. In certain preferred embodiments, a gel pad (e.g., in an array of gel pads) has a thickness of less than about 1 millimeter, 500 microns, 200, 100, 50, 40, 30, 20, 10, 5, or 1 microns.

It will be appreciated from the foregoing that a gel pad can entrap additional chemical species, if desired, e.g., to perform assays with or within the gel pad. For example, gels which include DNA probes have been used for SBH (for example, U.S. Patent No. 5,552,270 to Khrapko *et al.*). Thus, a gel pad can be prepared such that a chemical species is trapped within the gel pad, or a desired species can be added after the gel pad has been prepared, e.g., by contacting a preformed gel pad with a solution of the reagent and allowing the reagent to diffuse into the gel pad. Examples of reagents which can be entrapped, suspended or dissolved in a gel pad include proteins, such as enzymes (e.g., ligases, which can be useful

for positional SBH (see, e.g., Cantor, U.S. Patent Nos. 5,503,980 and 5,631,134)), polynucleotides, growth factors (e.g., for use with cells, e.g., see *infra*), salts and the like.

In one aspect, the invention provides methods for making gel pads and gel pad arrays. In certain preferred embodiments, gel pads and gel pad arrays can be conveniently prepared by use of "intelligent gels." Intelligent gels are gels which have properties which change (preferably reversibly) in response to changes in external conditions (for descriptions of certain intelligent gels, see, e.g., Kajiwara et al., "Synthetic Gels on the Move", *Nature*, vol. 355, pp. 208-209 (1992); Kwon et al., "Electrically Erodible Polymer Gel for Controlled Release of Drugs", Nature, vol. 354, pp. 291-293 (1991); Suzuki et al., "Phase Transition in Polymer Gels Induced by Visible Light", *Nature*, vol. 346, pp. 345-347 (1990); Osada et al., " Intelligent Gels" , *Scientific American*, pp. 82-87 (1993); R. Dagani, "Intelligent Gels," *Chem. Eng. News.*, June 9, 1997). Examples of intelligent gels include gels which become softer or firmer (e.g., solidify or liquefy) in response to changes in temperature, salt concentration (e.g., ionic strength), pH, exposure to radiation (e.g., ultraviolet (UV) radiation), presence or absence of a selected metal ion, electrical current, magnetic field, and the like. For example, a copolymer of poly(acrylic acid) and poly(N-isopropylacrylamide) has been reported to be temperature-sensitive, swelling at lower temperatures and collapsing at higher temperatures (Tanaka et al., *Faraday Discuss.* 101:201 (1995)). One of ordinary skill in the art will be able to select an intelligent gel with the desired properties for a selected application using no more than routine experimentation. In certain preferred embodiments, an intelligent gel for use in the present invention is responsive (e.g., liquefies) in response to an increase in temperature or irradiation with ultraviolet light.

Gel pad arrays can also be prepared by treating the surface of the substrate to create a pattern of alternating hydrophobic and hydrophilic sites on the surface. For example, a glass surface can be silated with a conventional silating reagent to prepare a patterned surface having hydrophobic and hydrophilic portions. A gel, such as an intelligent gel, is then poured onto the surface. A hydrophobic gel will be repelled by a hydrophilic surface, while a hydrophilic gel will be repelled by a hydrophobic surface. A patterned surface can be used to urge the liquefied gel into a pre-selected pattern on the substrate, thereby forming a gel pad array.

In another embodiment, a gel pad (e.g., in an array) can be prepared through the use of a derivatized monomer unit, followed by formation of the gel pad by polymerization of the monomer. For example, acrylic acid can be readily derivatized with a polynucleotide (e.g., a probe for use in SBH), e.g., by esterification. The resulting acrylic ester of the polynucleotide can then be disposed in an array format on a substrate, e.g., by dispensing a solution of the acrylic ester through a nozzle or array of nozzles (such as conventional piezoelectric ink-jet printing nozzles; see also Patent Cooperation treaty Publication WO95/04594). Alternatively, an array format can be provides by using a cast or mold. The

array of droplets is then polymerized *in situ* to provide an array of gel pads which incorporate a polynucleotide covalently bound to the gel polymer.

In one aspect, the invention provides gel pad arrays on flexible substrates, such as tapes. A variety of tapes can be employed as substrates for the gel pad arrays. Preferred tapes are biocompatible and/or compatible with test conditions, e.g., as are used for performing assays (to avoid interference with such assays). In addition, preferred tapes are relatively resistant to stretching, to reduce distortion of gel pad arrays deposited on the tape, e.g., during manufacture or storage of the tape. One preferred material for a tape substrate is polystyrene tape, which is commercially available from several suppliers.

A tape substrate can be transparent or translucent, and optionally includes a magnetic coating for information storage. The film can optionally be optically encoded.

If a tape having gel pad arrays disposed on a tape surface is wound up, gel material could potentially be transferred from one tape surface (e.g., the top surface) to another tape surface (e.g., the tape back) which is pressed against the first surface when the tape is wound. To prevent such transfer and consequent loss of gel pad integrity, the tape can be shaped or formed to have ridges or other structure along the length of the tape web. For example, as shown at the top of Figure 1, a tape can be provided with ridges along each edge, running along the length of the tape, to prevent contact between a gel pad and the layer of tape which is wound above the pad. This configuration ensures that the integrity of the gel pad will not be disturbed during storage of the tape.

The invention also provides a carrier for tapes which includes gel pad arrays. The carrier includes a housing, and at least one tape reel (more preferably two reels) for winding the tape. As shown in Figure 1, the tape carrier can resemble a conventional videotape housing, although the dimensions will vary depending upon factors such as the width, thickness, and length of the tape employed. In preferred embodiments, the housing includes a cover for closing the carrier, to thereby exclude light, moisture, dust, or other contaminants which could degrade the tape or the gel pads disposed thereon. The housing can optionally include visible or machine-readable indicia, such as a bar code or magnetic recording stripe, for storing information (such as date of manufacture, type of gel pad array, and the like) about the tape stored within the enclosure.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, numerous equivalents to the specific procedures described herein. Such equivalents are considered to be within the scope of this invention and are covered by the following claims.

The contents of all publications and patent applications described herein are hereby incorporated by reference.

Other embodiments are within the following claims.

What is claimed is:

1. A flexible tape having a gel pad array disposed on a surface of the tape.

2. The flexible tape of claim 1, wherein the tape comprises means for preventing compression of gel pads when the tape is wound on a reel.

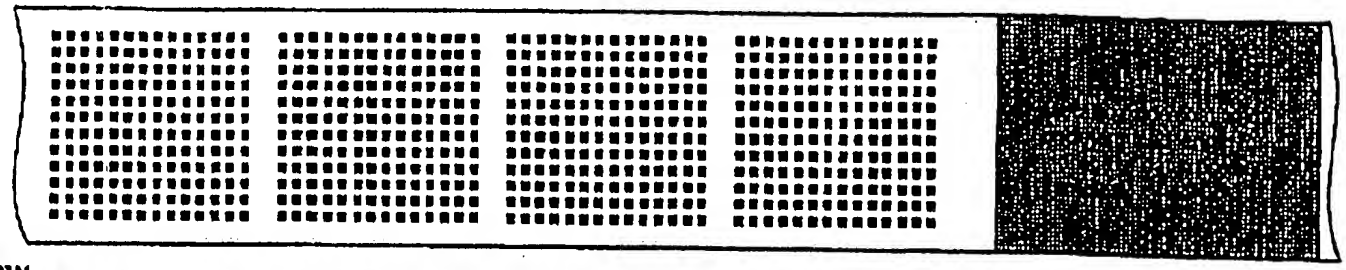
3. The flexible tape of claim 2, wherein the means for preventing compression comprises at least one ridge which extends along a length of the tape.

4. A carrier for a tape having gel pad arrays thereon, the carrier comprising a housing, at least one tape reel for winding the tape, and visible or machine-readable indicia for storing information about the tape stored in the carrier.

Abstract

Gel pads on flexible tape substrates, and carriers for storing them, are disclosed.

Top View



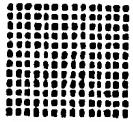
Side View

End View

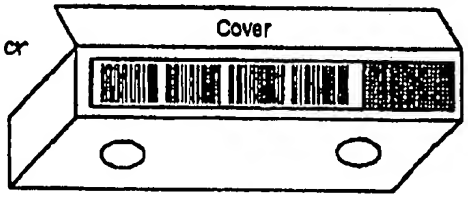
Gel pads on top surface of tape.

Preferably 1" tape or larger, but tape width can be varied.

Barrier strips on back side of film prevents gel pad compression. Also used to seal out contaminants and for tape handling during tape transport.

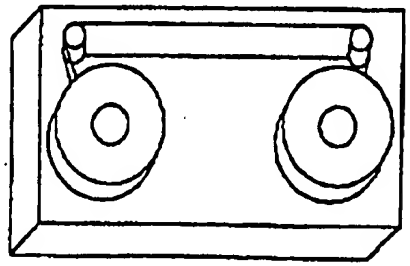


Gel Pad Array:
These acrylamide pads are adhered to the plastic in very high density arrays. Pads can be from 25um to 100um square and at spacing of 50um to 400um. The sizes and spacing of these pads and array dimensions can be varied for a particular use or instrument.



Film Carrier:
Plastic enclosure for storage and insertion into instrument. Bar coding on edge of carrier box of cataloging. Cover closes over end of array film in the carrier.

Overall Description:
Film used is non-rigid, transparent or translucent plastic which contains arrays of pads composed of acrylamide bound to the surface of the tape. Sections of the film optionally ferro-magnetic coating for magnetic storage of information on the film for position or sample information. Optical encoding onto the film may also be employed by a series of marks and spaces manufactured into the edge of the film. Film has a barrier strip along each edge of the back of the film for sealing and spacing to prevent array compression and for tape handling. Film enclosed into a case, similar to a VCR casette for handling and storage.



Inside view of film carrier

Figure 1

Component: 1 - Array Film and Carrier	Not to Scale